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10/543,063	03/09/2006	Stephen Keith Jones	03955.0152USWO	3902

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,063	JONES ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-22,25 and 28-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-22,25,28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 2/25/2010, in reply to the Office Action mailed 8/28/2009, is acknowledged and has been entered. Claims 1-4 and 8-10 have been amended. Claims 32-34 have been cancelled. Claims 1-4, 8-22, 25 and 28-31 are pending and are readable upon the elected invention and are examined herein on the merits for patentability.

Response to Arguments

Applicant's arguments regarding the rejection of claims 1, 9, 11-17, 19-22, 25, 28-31 and 33 under 35 U.S.C. 102(e) as being anticipated by Handy (US 6,997,863) have been fully considered and are persuasive because Handy does not teach a plurality of magnetic particles within a matrix. Therefore, the rejection has been withdrawn.

Applicant's arguments regarding other rejections set forth in the previous Office Action have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 9, 11-22, 25, 28, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Pouliquen ("Magnetite-Dextran Nanocapsules: Preparation and Properties," Microspheres, Microcapsules and Liposomes, 2001, 3, p. 495-523), for reasons set forth in the previous Office Action.

Applicant argues on pages 7-9 of the Response that Pouliquen teaches magnetite dextran nanocapsules (MDN) and relaxivity of nanocapsules, however it does not teach the microparticle composition or method of use of the present application. Applicant asserts that the technical implications of the particular values of SAR, VAR and W/g relate to the dynamic magnetic properties of the claimed compositions and such values are not taught or suggested by the cited reference. Applicant contends that magnetic characteristics are nanomagnetic particles are notoriously sensitive to variations and are not purely determined by their chemical composition. Parameters such as average particle size and size distribution impacts the ability of the claimed particles to be used in hyperthermia; surface characteristics and interaction effects between neighboring particles combine to determine how much heat (i.e. SAR, VAR) is produced under specific magnetic field conditions; and can only be achieved by

considering the microparticle construct as a whole. Applicant is of the opinion that none of the microparticle systems of the cited literature could achieve the . Applicant also asserts that it is important to consider effects of particle aggregation.

This is not found to be persuasive. First, it is noted that the intended use of a composition is not given patentable weight to distinguish over the cited prior art because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). It is further noted that with respect to VAR variables, that the pending claims are very broad and do not actually require a VAR value. For example, claim limitations (a), (b) and (c) are presented in the alternative; i.e. at least one of (a), (b) **or** (c). The compositions of Pouliquen meet the structural requirements required by the instant claims. With respect to applicant's arguments regarding aggregation, no claim limitations related to aggregation are set forth. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, Pouliquen even teaches the compositions to be useful for hyperthermia.

Claims 1-4, 9, 11-17, 19-22, 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Widder *et al.* (US 4,247,406), for reasons set forth in the previous Office Action.

Applicant argues on pages 9-10 of the Response that Widder describes microspheres with average size less than 1.5 micron with magnetic particles embedded therein, but that there is no teaching or suggestion for the use of these particles in hyperthermia treatment, no mention of specifically addressing any of the problems associated with trying to maximize heating, or any disclosure of the measurements of SAR and VAR; and no mention of the need to disperse the particles throughout the matrix to avoid aggregation.

This is not found to be persuasive. First, it is noted that the intended use of a composition is not given patentable weight to distinguish over the cited prior art because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). It is further noted that with respect to VAR variables, that the pending claims are very broad and do not actually require a VAR value. For example, claim limitations (a), (b) and (c) are presented in the alternative; i.e. at least one of (a), (b) **or** (c). The compositions of Widder meet the structural requirements required by the instant claims. With respect to applicant's arguments regarding aggregation, no claim limitations related to aggregation are set

forth. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 1-4, 9, 11-22, 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Chatterjee *et al.* (US 2004/0065969), for reasons set forth in the previous Office Action.

Applicant argues on page 7 of the Response that Chatterjee describes methods for microencapsulation of an agent where the agent could be magnetic nanoparticles of size of 5 to 50 nm. Up to 40% of the weight of the microparticles could be the agent and the microparticles can be up to 1000 nm in size. Applicant asserts that there is no teaching of using these particles for hyperthermia, no mention of specifically addressing problems associated with trying to maximize heating, no discussion of measurement of SAR or VAR and no need to disperse particles throughout the matrix to avoid aggregation.

This is not found to be persuasive. First, it is noted that the intended use of a composition is not given patentable weight to distinguish over the cited prior art because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the

intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). It is further noted that with respect to VAR variables, the pending claims are very broad and do not actually require a VAR value. For example, claim limitations (a), (b) and (c) are presented in the alternative; i.e. at least one of (a), (b) **or** (c). The compositions of Widder meet the structural requirements required by the instant claims. With respect to applicant's arguments regarding aggregation, no claim limitations related to aggregation are set forth. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 8-22, 25, 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray *et al.* (US 6,167,313) in view of Lesniak *et al.* (US 6,541,039) and Handy *et al.* (US 6,997,863), for reasons set forth in the previous Office Action.

Applicant argues on pages 10-11 of the Response that Gray does not teach magnetic material in the form of nanoparticles, but that the use of nanoparticles is different than other types of particles. Applicant asserts that nanoparticles have an extreme tendency to aggregate into clumps and that aggregation is an extreme case of particle interaction that according to applicant's experience will completely destroy the individual particles ability to heat under clinically acceptable magnetic field conditions. Applicant contends that in the composition claimed, magnetic nanoparticles disperse throughout the polymer matrix and do not form aggregated clumps within the matrix. Applicant assets that a higher concentration of nanoparticles within each microsphere is needed to achieve the required VAR, and refers to the need for dispersion in the specification.

This is not found to be persuasive. With respect to applicant's arguments regarding aggregation, no claim limitations related to aggregation are set forth. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, Applicant's specification at published paragraph 0048 describes that up to 90% of the particles within the matrix may aggregate. Applicant has not provided a clear showing that the compositions of Gray exhibit aggregation beyond this acceptable level,

especially since the synthetic methods of Gray in Example 1 are quite similar to the synthetic methods in the instant specification at Example 2.

Applicant further argues that the nano-scale particles of Lesniak and Handy are not the same as those claimed, such as Lesniak teaches a core or outer layers while the compositions claimed in the present invention comprise nanomagnetic particles distributed within a matrix; and that Lesniak does not teach SAR, VAR variables. Applicant argues that Handy is directed to a method based on a plurality of single domain nanomagnetic particles attched to a ligand, but does not teach nanomagnetic particles within a matrix, the required VAR or SAR, size or specific heating conditions.

This is not found to be persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Gray reference teaches the presence of superparamagnetic particles (preferably Fe_2O_3) within a matrix. The Lesniak and Handy references were relied upon to show that particle size of not more than 30 nm is usually a prerequisite for superparamagnetism (see Lesniak column 3, lines 60+), so this particle size would have been useful in the compositions of Gray. With regard to VAR variable, it is noted that the compositions of Gray have the same size, density and material components as those claimed and exemplified in Applicant's specification. The fact that Applicant has measured a physical property that was not explicitly recited in the prior art is not given patentable weight. It is interpreted that since

the compositions of Gray have same physical properties as those claimed, they would be capable of achieving the same functional properties. See MPEP 2112.

I. SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DIS-COVERY OF A NEW PROPERTY

"[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004).

In the instant case, the fact that Applicant has performed measurement of VAR values on compositions having the same physical characteristics does not render an old composition to be a novel composition.

Claims 1-4, 8-22, 25, 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones *et al.* (*Phys. Med. Biol.*, 2001, 46, p.385-398), for reasons set forth in the previous Office Action.

Applicant argues on pages 12-13 of the Response that Jones describes the use of microspheres formulated to contain non-superparamagnetic ferromagnetic particles, which are much larger than the nanomagnets used in the microparticles in the present application. Applicant argues that the articles highlights the problem the inventors have overcome by using nanomagnets, that is field strength used in the experiments described is 40 kA/m (approx 500 Oe), it is far greater than the 60 to 120 Oe claimed which is clinically acceptable. Applicant argues that Lesniak and Handy do not teach

nanoparticles dispersed in a matrix, and that further there is no disclosure of SAR, VAR, or preferred magnetic field conditions. Applicant further argues that the particles in Lesniak are suspended in a fluid medium and are designed to be readily imported directly into tumor cells and that by contrast the microparticle composition of the present invention is designed to be delivered to target site via intravascular infusion and hence to embolise capillary beds surrounding the target site.

This is not found to be persuasive. Jones teaches that the individual ferromagnetic particles have a particle size of less than 1 micrometer (page 388), and thus the magnetic particles are actually nanoscale. With regard to the argument that Lesniak and Handy do not teach particles distributed within a matrix, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the Jones reference teaches the presence of ferromagnetic particles (preferably Fe_2O_3) which are smaller than one micrometer within a matrix. The Lesniak and Handy references were relied upon to show the claimed particle size would have been useful in the compositions of Jones. With regard to VAR variable, it is noted that the compositions of Jones have the same size, density and material components as those claimed and exemplified in Applicant's specification. The fact that Applicant has measured a physical property that was not explicitly recited in the prior art is not given patentable weight. It is interpreted that since the compositions of Jones have same

physical properties as those claimed, they would be capable of achieving the same functional properties. See MPEP 2112. In the instant case, the fact that Applicant has performed measurement of VAR values on compositions having the same physical characteristics does not render an old composition to be a novel composition.

With regard to the argument that Lesniak does not teach embolization, Jones teaches embolization with his larger microspheres (see page 388, lines 21-22).

With regard to magnetic field operating frequency and field strength, Handy teaches the claimed magnetic field properties as known field conditions for use with thermotherapeutic magnetic compositions (column 8-9).

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is drawn to a microparticle composition of claim 1, wherein the microparticles within the composition have a size of about 25 nm to about 45 microns. However, the specification as originally filed does not appear to provide

support for the amended claims including the limitation that microparticles are in the size range of 25 nm to 45 microns. The specification was reviewed and describes that microparticles having a size range from 100 nm to 200 microns, preferably 10 microns to 50 microns, more preferably 20 to 45 microns and highly preferably from 25 to 37 microns at published paragraph 0073. Microparticles selected to have a size range 25-45 micron are disclosed at published paragraph 0116. However, there does not appear to be any disclosure that the microparticle is a small as 25 nm, as now claimed. If the examiner missed a passage in the specification which supports the limitations of the amended claim, Applicant is respectfully invited to direct the examiner's attention to the section of the specification that describes such limitations. This is a new matter rejection.

Claim Objections

Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim is drawn to a microparticle composition of claim 1, wherein the microparticles within the composition have a size of about 25 nm to about 45 microns. However, claim 1 recites a size range of about 100 nm to about 200 microns. Accordingly, the size range of claim 1 extends the lower limit of size of the microparticle, and fails to further limit the claim from which it depends.

Conclusion

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Tuesday and Thursday-Friday 9 AM-5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS